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510(k) Summary of Substantial Equivalence
Aperio Technologies, Inc.
(ScanScope® XT System)

OCT 31 2008

21 CFR 807.92(a):

21 CFR 807.92(a) (1):

Submitter's name and address:

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Date this 510(k) summary was prepared:

October 23, 2008

21 CFR 807.92(a)(2):

Trade Name of Device:	ScanScope® XT System
Regulatory Section:	21 CFR 864.1860 Immunhistochemistery reagents and kits
Classification:	Class II
Product Code:	OEO (automated digital image manual interpretation microscope)

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21 CFR 807.92(a)(3): Legally marketed predicate device to which substantial equivalence is claimed:

Predicate Device:	ScanScope® XT System
Manufacturer:	Aperio Technologies, Inc.
Predicate Device k#:	K071671

21 CFR 807.92(a)(4): Description of the device that is the subject of this premarket notification:

System: The system comprises a ScanScope® XT digital slide scanner instrument and a computer system executing Spectrum™ software. The system capabilities include digitizing microscope slides at diagnostic resolution, storing and managing the resulting digital slide images, retrieving and displaying digital slides, including support for remote access over wide-area networks, providing facilities for annotating digital slides and entering and editing metadata associated with digital slides, and facilities for image analysis of digital slides, including the ability to quantify characteristics useful to Pathologists, such as measuring and scoring immunohistochemical stains applied to histology specimens, such as Dako PR, which reveal the presence of PR (Progesterone Receptor) protein expression, which may be used to determine patient treatment for breast cancer.

Hardware Operation: The ScanScope XT digital slide scanner creates seamless true color digital slide images of entire glass slides in a matter of minutes. A high numeric aperture 20x, as found on conventional microscopes, is used to produce high-quality images. (When the 2X magnification changer is inserted, the effective magnification of the images is 40X.) The ScanScope XT employs a linear-array scanning technique that generates images free from optical aberrations along the scanning axis. The result is digital slide images that have no tiling artifacts and are seamless.

Software Operation: The Spectrum software is a full-featured digital pathology management system. The software runs on a server computer called a Digital Slide Repository (DSR), which stores digital slide images on disk storage such as a RAID array, and which hosts an SQL database that contains digital slide metadata. Spectrum includes a web application and services which encapsulate database and digital slide image access for other computers. The Spectrum server supports the capability of running a variety of image analysis algorithms on digital slides, and storing the results of analysis into the database. Spectrum also includes support for locally or remotely connected image workstation computers, which run digital slide viewing and analysis software provided as part of Spectrum.

Overview of System Operation: The laboratory technician or operator loads glass microscope slides into a specially designed slide carrier with a capacity of up to 120 slides. The scanning process begins when the operator starts the ScanScope scanner and finishes when the scanner has completed scanning of all loaded slides. As each glass slide is processed, the system automatically stores individual "striped" images of the tissue contained on the glass slide and integrates the striped images into a single digital

slide image, which represents a histological reconstruction of the entire tissue section. After scanning is completed, the operator is able to view and perform certain analytical tests on the digital slides.

21 CFR 807.92(a)(5): Intended use and labeled indications for use:

The ScanScope® System is an automated digital slide creation, management, viewing and analysis system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape.

The IHC PR Manual Read of Digital Slides application is intended for use as an aid to the pathologist in the detection and quantitative measurement of PR (Progesterone Receptor) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for PR on a computer monitor.

It is indicated for use as an aid in the management, prognosis, and prediction of therapy outcomes of breast cancer.

21 CFR 807.92(a)(6): Technological characteristics:

The design, construction, energy source and other characteristics of the ScanScope System candidate device are considered to be substantially equivalent to the relevant features of the predicate device. A summary of the technological characteristics of the ScanScope System candidate device in comparison to the predicate device follows:

Method of cell detection. The method of cell detection is by colorimetric and morphometric pattern recognition by microscopic examination of prepared cells by size, shape, color, and intensity as observed by a computer-automated, microscopic digital slide scanner system and/or by visual observation by a health care professional.

System Components. The system components comprising the ScanScope System candidate device are substantially equivalent to those in the predicate device; i.e., a computer-automated digital microscope slide scanner, computer, color monitor, and keyboard.

Energy Source. The electrical service is 100vAC – 240vAC, 50Hz/60 Hz, 2 amps which is similar to the predicate device electrical service requirements.

21 CFR 807.92(b): 510(k) summaries for those premarket submissions in which determination of substantial equivalence is also based on an assessment of performance data shall contain the following information:

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21 CFR 807.92(b)(1): Brief discussion of non-clinical tests submitted, referenced or relied on in this premarket notification:

There are no non-clinical tests submitted, referenced or relied on in this submission.

21 CFR 807.92(b)(2): Brief discussion of clinical tests submitted, referenced or relied on in this premarket notification:

Comparison studies:

a. Method comparison with predicate device:

The substantial equivalence study was based on comparison of reading digital slides on a computer monitor to reading glass slides using conventional manual microscopy. Manual microscopy and the manual reading of digital slides on a computer monitor were performed in accordance with the reagent vendor's instructions for use.

Two Clinical Laboratory Improvement Amendments (CLIA) qualified clinical sites participated in the study. Prior to their participation in the study each clinical site obtained exemption status from an Institutional Review Board (IRB).

A total set of 180 formalin-fixed, paraffin-embedded breast tissue specimens from both clinical sites were used for the PR study; 80 slides from the first clinical site and 100 slides from the second clinical site.

The specimens at the first clinical site were selected based on their clinical scores on file to provide an equal distribution of PR slides in the percentage of positive nuclei ranges 0%, 1% to 4%, 5% to 9%, 10% to 49%, and 50% to 100%. The specimens at the second clinical site were routine specimens taken from their clinical operation, representing the true target population of cases in a typical clinical setting.

All specimens for the PR study were immunohistochemically stained at the clinical sites using Dako in vitro diagnostic (IVD) FDA cleared Monoclonal Mouse Anti-Human Progesterone Receptor (Clone PgR 636) (K020023).

The study was performed primarily at the participating clinical sites and all parts except the scanning of glass slides were performed at their facilities using their typical workflow. The glass slides were prepared in the sites' clinical laboratories and read by board certified staff pathologists. For the scanning of glass slides ScanScope XT instruments were operated in a simulated clinical setting at Aperio (designed to be representative of a typical lab environment).

All ScanScope XT instruments used in the study were production units and were delivered, installed, and maintained in accordance with the approved procedures, per Aperio's QSPs (Quality Systems Procedures), and as described in product documentation and labeling.

Three different board-certified pathologists at each clinical site performed a blinded manual review of each glass slide using a conventional light microscope. The pathologists reported the percentage of positive nuclei [0%, 1%, ... 100%] and average intensity score of 0, 1+, 2+ or 3+ for each of the reviewed glass slides.

Based on the manual microscopy average percentages of positive nuclei from the three pathologists, the glass slides used for the PR study provided the following percentages of positive nuclei distribution.

Percentage	Clinical Site 1	Clinical Site 2	Total
0%	29	33	62
[1%- 5%)	12	6	18
[5%-10%)	8	3	11
[10%-50%)	15	11	26
[50%-100%]	16	47	63
Total	80	100	180

PR Percentage of Positive Nuclei Distributions.

Based on the manual microscopy average intensity scores from the three pathologists, the glass slides used for the PR study provided the following average intensity score distribution.

Intensity Score	Clinical Site 1	Clinical Site 2	Total
0	26	31	57
1+	14	3	17
2+	20	12	32
3+	20	54	74
Total	80	100	180

PR Average Intensity Score Distributions.

As it can be seen from the PR percentage of positive nuclei distribution, it was not possible to obtain an equal distribution of the percentage of positive nuclei in the range from 1% to 10%. This difficulty was founded in the limited representation of this percentage range in the true target population of cases.

All glass slides were scanned using a different ScanScope XT instrument for each clinical site.

After a wash-out period of over one week and subsequent randomization of the slides, the same three Pathologists at each clinical site performed a blinded manual read of each digital slide displayed on a computer monitor using the ScanScope XT System's remote viewing capability. The pathologists reported the percentage of positive nuclei [0%, 1%, ... 100%] and average intensity score of 0, 1+, 2+ or 3+ for each of the reviewed digital slides.

The statistical analyses are presented for each of the scores: percentage of positive nuclei and intensity scores. The statistical analyses are presented across all slides for manual microscopy and manual reading of digital slides on a computer monitor, and comparatively between the two methods for the clinical sites with their different three pathologists.

Percentage of Positive Nuclei - Progesterone Receptor (PR)

The inter-pathologist agreements for reading digital slides were in the range of 76.3%-98.0% and the inter-pathologist agreements for manual microscopy were in the range of 83.8%-99.0%.

The agreements between the pathologists' manual microscopy and reading digital slides were in the range of 78.8%-100.0% and the inter-pathologist agreements for manual microscopy were in the range of 83.8%-99.0%

Intensity Score - Progesterone Receptor (PR)

The inter-pathologist agreements for reading digital slides were in the range of 58.8%-78.0% and the inter-pathologist agreements for manual microscopy were in the range of 58.8%-88.0%.

The agreements between the pathologists' manual microscopy and reading digital slides were in the range of 62.5%-96.0% and the inter-pathologists agreements for manual microscopy were in the range of 58.8%-88.0%.

Analytical Performance:

a. Precision/Reproducibility:

The precision of the ScanScope XT System was determined in a suite of intra-system, inter-day/intra-system, inter-system, intra-pathologist and inter-pathologist studies.

To measure the precision and reproducibility of the system for the manual reading of digital slides, an image analysis algorithm was used that detects and quantifies the same cell features and uses the same scoring scheme as the pathologists. This method allowed the quality of the digital slides to be quantified objectively in terms of their interpretability for PR scoring, and enabled detection of small variations of the system humans would not be able to detect.

10 PR slides from the comparison study were used for this study. The PR slides consisted of formalin-fixed, paraffin-embedded breast tissue specimens immunohistochemically stained using Dako in vitro diagnostic (IVD) FDA cleared Monoclonal Mouse Anti-Human Progesterone Receptor (Clone PgR 636) (K020023).

The pathologists' selection of tumor regions for image analysis introduces some variability to the system. To properly assess the true variability of the system the influence of the pathologists' selections in the intra- system and inter-systems studies was eliminated by using the same tumor regions for image analysis of all scans of the same slide.

The image analysis algorithm reported the percentage of positive nuclei [0.0%, ... 100.0%] and average intensity score of 0, 1+, 2+, or 3+ as well as the underlying average intensity on a scale from 0 to 255.

The statistical analyses are presented for the percentage of positive nuclei and intensity values.

Intra- system: The slide scores provided by image analysis over 10 consecutive scans were analyzed for all 10 PR slides.

Percentage of Positive Nuclei

The image analysis results show an overall standard deviation of 0.54% (maximum 1.47%) and average range (maximum – minimum) of 1.06% (maximum 4.78%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

Intensity Values

The image analysis results show an overall standard deviation of 0.9 (maximum 1.60) and average range (maximum – minimum) of 2.48 (maximum 4.27) for the intensity values [0-255] across all runs.

Inter-day/intra-system: The slide scores provided by image analysis over 20 scans on different days were analyzed for all 10 PR slides.

Percentage of Positive Nuclei

The image analysis results show an overall standard deviation of 0.54% (maximum 1.09%) and average range (maximum – minimum) of 1.52% (maximum 3.90%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

Intensity Values

The image analysis results show an overall standard deviation of 1.44 (maximum 2.43) and average range (maximum – minimum) of 5.29 (maximum 11.39) for the intensity values [0-255] across all runs

Inter-system: The slide scores provided by image analysis over 10 consecutive scans on three different ScanScope XT instruments were analyzed for all 10 PR slides.

Percentage of Positive Nuclei

The image analysis results on each of the three ScanScope systems show an overall average standard deviation of 0.54%, 0.53% and 0.75% (maximum 1.47%, 1.23%, 2.05%) and average range of 1.06%, 1.23%, and 1.50% (maximum 4.78%, 4.17%, 7.20%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

The image analysis results of the three ScanScope systems combined show an overall average standard deviation of 0.87% (maximum 1.57%) and average range of 2.54% (maximum 8.13%) for the percentage of positive nuclei [0.0-100.0%] across all runs.

The image analysis results show minimal variation from one ScanScope system to another as shown in the following table that shows the mean over all runs of the reported percentage of positive nuclei [0.0-100.0%] for the 10 PR slides (#S) for the three ScanScope systems.

	S#1	S#2	S#3	S#4	S#5	S#6	S#7	S#8	S#9	S#10
ScanScope #1	0.00	0.11	0.20	1.54	3.72	12.77	18.14	35.01	46.90	73.09
ScanScope #2	0.00	0.12	0.14	1.59	4.44	12.64	17.75	35.21	47.28	72.15
ScanScope #3	0.00	0.13	0.10	1.52	2.52	10.34	18.00	33.13	45.72	71.06

Intensity Values

The image analysis results on each of the three ScanScope systems show an overall average standard deviation of 0.9%, 1.01%, and 0.93% (maximum 1.60%, 1.64%, 1.48%) and average range of 2.48%, 2.62%, and 2.60% (maximum 4.27%, 5.09%, 4.85%) for the intensity values [0-255] across all runs.

The image analysis results of the three ScanScope systems combined show an overall average standard deviation of 1.35% (maximum 2.03%) and average range of 4.55% (maximum 6.86%) for the intensity values [0-255] across all runs.

The image analysis results show minimal variation from one ScanScope system to another as shown in the following table that shows the mean over all runs of the reported percentage of positive nuclei [0.0-100.0%] for the 10 PR slides (#S) for the three ScanScope systems.

	S#1	S#2	S#3	S#4	S#5	S#6	S#7	S#8	S#9	S#10
ScanScope #1	N/A	N/A	N/A	160.10	203.65	191.84	186.11	176.15	148.62	139.88
ScanScope #2	N/A	N/A	N/A	160.00	204.05	191.61	184.07	175.62	149.26	141.15
ScanScope #3	N/A	N/A	N/A	160.45	202.57	191.68	185.53	175.91	152.69	143.52

Intra-Pathologist: One pathologist read the same 10 PR slides 5 times using manual microscopy and 5 times using a manual read of digital slides on a computer monitor.

Percentage of Positive Nuclei

The manual microscopy results show an overall average standard deviation of 6.73% (maximum 16.73%) and average range of 9.8% (maximum 40%) and the manual read of digital slides results show an overall average standard deviation of 11.81% (maximum 28.72%) and average range of 16.2% (maximum 75%).

Intensity Scores

The manual microscopy results show 8 outliers out of 50 scores (16%) and the manual read of digital slides results show 9 outliers out of 50 scores (18%). Outliers are defined as scores that are different from the median values of the scores provided by the pathologist over 5 runs of the method.

Inter-pathologist: Three pathologists read the same 10PR slides using manual microscopy and using a manual read of digital slides on a computer monitor (based on the data from the clinical comparison to manual microscopy study).

Percentage of Positive Nuclei

The manual microscopy results show an overall average standard deviation of 13.30% (maximum 32.15%) and average range of 17.2% (maximum 60%) and the manual read of digital slides results show an overall average standard deviation of 11.3% (maximum 20.82%) and average range of 16.0% (maximum 40%).

Intensity Scores

The manual microscopy results show 7 outliers out of 30 scores (23%) and the manual read of digital slides results show 7 outliers out of 30 scores (23%). Outliers are defined as scores that are different from the median values of the scores provided by the three pathologists.

21 CFR 807.92(b)(3): Conclusions drawn from the non-clinical and clinical tests:
Based on the results of the clinical studies described in this 510(k) submission, it is concluded that the ScanScope System device is as safe and effective (therefore substantially equivalent) as the predicate device as an aid in the management, prognosis, and prediction of therapy outcomes of breast cancer.

....End of 510(k) Summary....

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Aperio Technologies, Inc.
c/o Kim Bloom
1430 Vantage Court, Suite 106
Vista, California 92081

OCT 31 2008

Re: k080254
Trade/Device Name: ScanScope® XT System
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry Reagents & Kits
Regulatory Class: Class II
Product Code: OEO
Dated: October 02, 2008
Received: October 03, 2008

Dear Ms Bloom:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed

predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

for Marian Chan, PhD
Acting Division Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

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Indications for Use

510(k) Number (if known): K080254

Device Name: ScanScope® XT System

Indications for Use:

The ScanScope® System is an automated digital slide creation, management, viewing and analysis system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size, pattern and shape.

The ScanScope® system is intended for use as an aid to the pathologist in the detection and quantitative measurement of PR (Progesterone Receptor) by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for PR on a computer monitor.

It is indicated for use as an aid in the management, prognosis, and prediction of therapy outcomes of breast cancer.

Prescription Use ___X___ (Part 21CFR 801 Subpart D)	AND/OR	Over-The-Counter Use _____ (Part 21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety 510(k) K080254